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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/482,682	01/14/2000	Daniel J. Von Seggern	22908-1235B	7337

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EXAMINER
FOLEY, SHANON A

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 09/09/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/482,682	VON SEGGERN ET AL.	
	Examiner	Art Unit	
	Shanon Foley	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 April 2003 and 27 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-23,41,47,69 and 95-103* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,6-9,11-13,15-18,20-23,41,47,69, 95-100, 102, 103* is/are rejected.

7)☒ Claim(s) *5,10,14,19 and 101* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *29* .
4) ☒ Interview Summary (PTO-413) Paper No(s). *31* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

In paper no. 26, applicant amended claims 1, 2, 4-6, 9, 10, 12, 21-23, 47, 96, 97, 99, cancelled claims 3, 24-40, 42-46, 48-68, 71-94 and added new claims 100-103. In paper no. 30, applicant amended claims 2, 12 and 101. Claims 1, 2, 4-23, 41, 47, 69 and 95-103 are under consideration.

Upon reconsideration, previously indicated as allowable subject matter is withdrawn.

Continued Prosecution Application

The request filed on 4/14/03 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/482682 is acceptable and a CPA has been established. An action on the CPA follows.

On page 2-3 of paper no. 30, applicant states the inventorship of the instant application may have changed due to cancellation of claims in paper no. 26 and is currently investigating the issue. The Office will presume that the inventorship is intact until applicant formally requests a change of inventorship.

Priority

According to the priority statement of 4/22/03, it appears that the claimed subject matter defined in the instant application is supported by the parent application serial nos: 09/423,783, PCT/EP97/05251 (corresponding to WO 98/13499) and 08/719,806. Based on the information given by applicant and an inspection of the patent applications, the examiner has concluded that some of the subject matter (explained below) is defined in this application is supported by the disclosure in application serial nos. 09/423,783 filed

November 12, 1999, PCT/EP97/05251 (corresponding to WO 98/13499) filed September 24, 1997 and 08/719,806, filed September 25, 1996.

The main concept within the instant claims is a nucleic acid having the same or different tripartite leader (TPL) exon sequences. This concept can be interpreted a number of ways:

1) When the TPL exons are different, i.e. TPL 1, 2, 3, but from the same adenovirus, support for this concept is found plasmid pCLF, disclosed in the parent applications discussed above.

2) When the TPL exons are the same, e.g. TPL 2, 2, 2, from the same or different adenovirus, implied support for this concept is found for example on page 36, lines 12-20 and examples 5 and 6 on pages 92-96 of the instant application, but cannot be located in any of the parents.

3) When the TPL exons are from the same or different adenoviruses, but are mixed up, e.g., Ad5 TPL2, Ad3 TPL 2, Ad5 TPL2 or Ad5 TPL3, Ad3 TPL 2, Ad5 TPL1 or Ad5 TPL2, Ad5 TPL 2, Ad5 TPL1, implied support for this concept is also found in the instant application on page 36, lines 12-20 and examples 5 and 6 on pages 92-96, but cannot be located in any of the parents.

Accordingly, the subject matter defined in the claims as interpreted in 1) above has an effective filing date of September 25, 1996. However, the concepts discussed in 2) and 3) above have an actual filing date of 1/14/2000, which is the filing date of the instant application.

Should applicant disagree with the examiner's factual determination above, it is incumbent upon the applicant to provide the serial number and specific page number(s)

of any parent application which specifically supports the particular claim limitation for each and every claim limitation in all the pending claims which applicant considers to have been in possession of and fully enabled for prior to 1/14/2000.

Application no: 09/795,292 is not available for consideration at the present time, so there is no way to determine if the subject matter instantly claimed would find support in the '292 application or not. Applicant is requested to provide the specific page number(s) of the '292 application which specifically supports the particular claim limitation for each and every claim limitation in all the pending claims which applicant considers to have been in possession and fully enabled for as of January 14, 1999.

Drawings

Formal drawings were received on 4/18/03. These drawings are acceptable.

Information Disclosure Statement

The examiner lined through a few of the US applications listed by applicant in the IDS submitted 4/18/3 because the application numbers could not be determined or the applications were unavailable.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9, 18, 100, 102 and 103 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled

in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that pCLF, pDV60, pDV67, pDV69, pDV80 and pDV90 are required to practice the claimed invention because they are required elements of the claims. As a required element it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, a deposit of the instant plasmids may satisfy the enablement requirements of 35 U.S.C. § 112, first paragraph. See 37 CFR 1.802.

The specification does not provide a repeatable method for obtaining pCLF, pDV60, pDV67, pDV69, pDV80 and pDV90 and it is not apparent if it is readily available to the public. Applicant's deposit statement in the specification bridging pages 88-89 does not indicate the extent of public availability. The MPEP § 2404.01 states that: "A mere reference to a deposit of biological material itself does not necessarily mean that the biological material is readily available." If the deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Logan et al. (Proc. Natl. Acad. Sci. 1994; 81: 3655-3659) or in the alternative Sheay et al. (Biotechniques. 1993; 15 (5): 856-862) for reasons of record.

The claims are drawn to a nucleic acid in a plasmid comprising an adenovirus TPL nucleic acid sequences comprising the first, second, and third TPL exons, such that at least two exons are different or the first and second TPL exons are different.

Logan et al. teaches that plasmid pJAW 43 encodes adenovirus type 2 tripartite leader sequences and plasmid pE1A-WT encodes rearranged E1A genes and 5' tripartite leader segments, see the first paragraph in the materials and methods section in column 1 on page 3655.

Sheay et al. teaches plasmid pRD112a, which encodes adenovirus type 2 tripartite leader sequences, see Figure 1.

Applicant argues that claim 1 requires that at least two of the exons are different, that is, "not normally found together in nature" (recited from page 34, lines 23-25 of the disclosure). Applicant concludes that neither Logan et al. nor Sheay et al. anticipate claims 1 and 11.

Applicant's arguments and citation have been fully considered, but are found unpersuasive. The excerpt pointed to in the specification by applicant is discussing a

generic recombinant DNA molecule and does not mention TPL exons. The TPL exons of Logan et al. or Sheay et al. are different. That is, the TPL exons 1, 2 and 3 of Logan et al. or Sheay et al. are differentially designated 1, 2 and 3. Therefore, none of the TPL exons of Sheay et al. or Logan et al. are the same. It is noted in the second paragraph on page 7 of the response filed 12/19/01 that applicant asserted "One of ordinary skill in the art would understand that the meaning of "different" is "not the same." Therefore, "different" as used in the claims means that the TPL exons may be from different adenoviruses or alternatively be from the same adenovirus as long as they are not the same TPLs." From applicant's clarification of what "different" means, it is clearly evident that the plasmid encoding adenovirus TPL sequences taught by Logan et al. or Sheay et al. clearly anticipate claims 1 and 11.

Claims 1, 2, 4 and 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Kaufman (PNAS. 1985; 82: 689-693).

Claims 1 and 11 are drawn to a nucleic acid in a plasmid comprising an adenovirus TPL nucleic acid sequences comprising the first, second, and third TPL exons, such that at least two exons are different or the first and second TPL exons are different. Claims 2 and 4 state that the TPL sequence is linked to adenovirus intron 1.

Kaufman teaches plasmid pD20 which contains the 2nd and 3rd exon sequences and the 5' splice site from the adenovirus 1st late leader sequence. Kaufman also teaches plasmid pD15 containing the same sequences as those in pD20, except that the exons are in opposite orientation with respect to the direction of transcription. Kaufman also teach plasmids comprising the entire adenovirus TPL sequence. See the "Plasmid Construction" bridging pages 689-690 and figure 1.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 6-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sheay et al. as applied to claims 1 and 11 above or, in the alternative, Kaufman as applied to claims 1, 2, 4 and 11 above, and further in view of Curiel (US 5,871,727).

Claims 6-8 are drawn to an isolated nucleic acid comprising TPL exons 1-3, a promoter and a sequence encoding an Ad3 head domain and an Ad5 tail domain.

See the teachings of Sheay et al. or Kaufman above. Neither reference teaches a sequence encoding an Ad3 head domain and an Ad5 tail domain.

Curiel teach a plasmid comprising a chimeric fiber gene encoding the tail of Ad5 and the head of Ad3, see Figure 13, column 16, line 64 to column 17, line 34 and column 24, lines 49-67.

One of ordinary skill in the art at the time the invention was made would have been motivated to combine the TPL sequences of Sheay et al. or Kaufman with the chimeric adenovirus fiber gene of Curiel to increase the translational efficiency of the heterologous chimeric fiber sequences of Curiel, see the abstract and the last paragraph of Kaufman, or to enhance expression of the chimeric construct, see Table 1 of Sheay et al. One of ordinary skill in the art at the time the invention was made would also have been motivated to express the chimeric fiber gene of Curiel using the TPL sequences of Sheay et al. or Kaufman to retarget recombinant adenoviruses, see the previous citations of

Curiel. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of combining the TPL sequences of Sheay et al. or Kaufman with the chimeric adenovirus fiber gene of Curiel because TPL sequences are present in native adenoviruses to express adenovirus genes and the chimeric fiber gene of Curiel is derived from adenoviruses. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Claims 12, 13, 15-17, 20-23, 41, 47, 69 and 95-97 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sheay et al. and Curiel as applied to claims 1, 6-8 and 11 above or Kaufman and Curiel as applied to claims 1, 2, 4, 6-8 and 11 above, and further in view of Wickham et al. (US 5,770,442).

Claims 12, 13 and 15-17 are drawn to an adenovirus packaging cell line comprising a stably integrated nucleic acid molecule comprising the nucleic acid of claims 6-8. Claims 20-23 state that the cell expresses an early protein and a fiber gene under an inducible promoter. Claims 41, 47, 95-97 are drawn to a method of producing an adenovirus particle by providing a packaging cell line comprising the instant stably integrated nucleic acid comprising TPL exons 1-3 and a fiber protein that produces adenovirus particles by complementation. Claim 69 lists specific cell lines.

See the teachings of Sheay et al. and Curiel or Kaufman and Curiel above. Neither combination of reference teaches a packaging cell line that expresses an early protein and a fiber gene under an inducible promoter or a method of producing an adenovirus particle.

Wickham et al. teach that 293 cells complement the E1 region of the adenovirus genome. Wickham et al. also teach transfecting a recombinant gene to be stably expressed in the cell line that is used to generate recombinant adenovirus by homologous recombination. See column 7, line 63 to column 8, line 11, column 9, line 61 to column 10, line 3, column 11, line 57 to column 12, line 23 and column 13, lines 1-37.

One of ordinary skill in the art at the time the invention was made would have been motivated to complement the chimeric fiber gene of Curiel by homologous recombination in 293 cells, taught by Wickham et al. to efficiently propagate adenoviruses with altered viral tropism, see the previous citations of Curiel et al. and column 7, line 63 to column 8, line 11 of Wickham et al. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for complementing the chimeric fiber gene of Curiel into the 293 cells of Wickham et al. because Wickham et al. specifically teach expressing genes required to homologously recombine genes to propagate retargeted adenoviruses from a complementing cell line. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Claims 98 and 99 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sheay et al., Curiel and Wickham et al. as applied to claims 1, 6-8, 11-13, 15-17, 20-23, 41, 47, 69 and 95-97 or Kaufman, Curiel and Wickham et al. as applied to claims 1, 2, 4, 6-8, 11-13, 15-17, 20-23, 41, 47, 69 and 95-97 above, and further in view of Branellec et al. (US 6,410,011 B1).

Claims 98 and 99 state that the adenovirus particle comprises a suicide gene.

See the teachings of Sheay et al., Curiel and Wickham et al. or Kaufman, Curiel and Wickham et al. Neither set of references teach an adenovirus particle comprising a suicide gene.

However, Branellec et al. teach an adenovirus comprising a suicide gene, see examples 1 and 2 bridging column 8, line 15 to column 9, line 60.

One of ordinary skill in the art at the time the invention was made would have been motivated to insert a suicide gene into the adenovirus of Sheay et al., Curiel and Wickham et al. or Kaufman, Curiel and Wickham et al. to inhibit proliferation of vascular smooth muscle cells, see claim 1 of Branellec et al. One of ordinary skill in the art at the time the invention was made would also have been motivated to insert a suicide gene into the adenovirus construct of Sheay et al., Curiel and Wickham et al. or Kaufman, Curiel and Wickham et al. to increase the translational efficiency of the heterologous sequences, see the abstract and the last paragraph of Kaufman, or to enhance expression of the heterologous sequences, see Table 1 of Sheay et al. One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation for producing an adenovirus of Sheay et al., Curiel and Wickham et al. or Kaufman, Curiel and Wickham et al. comprising a suicide gene because the insertion site of the suicide gene, taught Branellec et al. does not interfere with the TPL sequences of Sheay et al. or Kaufman or the chimeric fiber taught by Curiel. Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results to the contrary.

Allowable Subject Matter

Claims 5, 10, 14, 19 and 101 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. The prior art does not teach or suggest SEQ ID NO: 32, SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 47, SEQ ID NO: 64, SEQ ID NO: 65, SEQ ID NO: 26 or SEQ ID NO: 8.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shanon Foley whose telephone number is (703) 308-3983. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on (703) 308-4027. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Shanon Foley